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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,693	10/16/2001	Jonathan S. Stamler	Duke 1931	3762

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Ivor R. Elrifi, Esq.
Mintz, Levin, Cohn, Ferris Glovsky and Popeo PC
One Financial Center
Boston, MA 02111

EXAMINER

LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 04/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/977,693

Applicant(s)

STAMLER, JONATHAN S.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5-9, 11 and 12 is/are pending in the application.
4a) Of the above claim(s) 11 and 12 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-3 and 5-9 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

in

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed January 13, 2005.

Amendments were made to the claims.

Claims 1-3, 5-9, 11 and 12 are pending in the instant application. Claims 11 and 12 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-3 and 5-9 are under consideration in the instant application. Any rejection of record in the previous Office Action, mailed July 13, 2004, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

This application contains claims 11 and 12, drawn to an invention nonelected with traverse in the response filed May 19, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-3 and 5-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection. **This rejection is necessitated by amendment of the claims.**

Specifically, the phrase “screening for a proteomic interaction *between at least one protein and a plurality of proteins*” (emphasis added to indicate the amended portion of the phrase in question) represents New Matter with respect to the broad meaning of “proteomic interaction” as defined in the specification. In support of the instant amendment, Applicant points to the specification at page 1, line 5 and lines 15-18, page 7, lines 9-21, page 9, lines 16-17, page 9, line 21 to page 10, line 3, page 14, lines 9-12, page 19, lines 10-18, page 20, lines 14-18 and Examples I-IV.

First, it is noted that the specification defines “proteomic interaction” as meaning “change in level of expression of proteins or change in the interaction between proteins or change in the interaction between proteins and other molecules (e.g., DNA, RNA, lipids) or change in the activity of proteins” (see page 4, lines 10-12 of the instant specification). Thus, mapping “proteomic interactions” is much broader in scope than measuring the interaction between one protein and a plurality of proteins, including measuring the change in activity and expression of such proteins. Thus, in order for the instant amendment to find support in the instant specification, the broad scope of “screening for a proteomic interaction between at least one protein and a plurality of proteins” must find support in the specification. In this respect, it

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is set forth by the Office that the specification does not find support for the broad scope of the term "proteomic interactions" as defined by the specification.

No clear support is found on pages 1, 7, 14, 19 or 20 for the term "screening for a proteomic interaction between at least one protein and a plurality of proteins," as had been indicated by Applicant. At best, the instant specification provides support for measuring the interaction between "*at least one protein and a plurality of proteins*" by two-hybrid protein-protein interaction systems (see for example pages 9-10, and Examples I-IV, as indicated by Applicant). There is no support for measuring "proteomic interactions" between "*at least one protein and a plurality of proteins*" as it regards measuring a change in level of expression, a change in the interaction between proteins and other (non-protein) molecules, or a change in activity. As such, the amendment constitutes New Matter with regard to the full scope of the term "proteomic interactions."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Cominacini *et al.*

(*Free Radical Biology & Medicine* **22**: 117-127, 1997; see entire document; henceforth

Cominacini). **This rejection is necessitated by amendment of the claims.**

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First, it is again noted that the term “proteomic interactions” includes “change in level of expression of proteins” (see page 4, lines 10-12 of the instant specification). Thus, a method where “a plurality of proteins” are measured for change in level of expression in the presence and absence of a simulated redox state is within the broad scope of screening for “proteomic interactions between at least one protein and a plurality of proteins.”

Cominacini teaches measuring the expression levels of intercellular cell adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and E-selectin in response to an altered redox state (see for example the Abstract and Figure 3). Specifically, human umbilical vein endothelial cells (HUVECs) are cultured in the presence and absence of oxidized LDL protein, and the expression of ICAM-1, VCAM-1 and E-selectin are measured (see for example page 121, left column and Figure 3). The levels of expression of ICAM-1, VCAM-1 and E-selectin are measured in the presence of oxidized LDL protein (i.e., the presence of a simulated redox state perturbation), and are then calculated as a percent variation from the level of their expression in the absence of oxidized LDL (i.e., the absence of a simulated redox state perturbation) (see for example the legend for Figure 3, particularly the sentence bridging the columns) to represent the “proteomic map” between these proteins. It is additionally noted that the addition of oxidized LDL represents a variation of concentration of redox state modifier molecules from physiological state (as present in claim 2), and that the oxidized molecule is specifically a lipid peroxide (as present in claim 3). Thus, Cominacini anticipates the indicated claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishiyama (cited in the previous Office Action in a rejection under 35 USC § 102(b)). **This rejection is necessitated by amendment of the claims.**

Nishiyama teaches a method whereby the yeast two-hybrid system was used to identify the interaction between TRX and several candidate proteins, identifying three different candidate genes (see for example page 21646, right column, last paragraph). Nishiyama then explores the "proteomic interactions" between TRX and one candidate, TBP-Z, under redox conditions (see for example page 2 1647, left column, bottom paragraph and Figure 3). Specifically, Nishiyama shows that the interaction between TRX and TBP-2 is inhibited by the presence of the redox agents diamide and hydrogen peroxide (again see for example page 21647, left column, bottom paragraph and Figure 3).

Nishiyama does not explicitly teach measuring the "proteomic interactions" in the presence and absence of redox state modifiers between TRX and the remaining candidate proteins (i.e., between one protein (TRX) and a plurality of proteins) with which it was found to interact (again see for example page 21646, right column, last paragraph). However, it would have been obvious for the ordinary skilled artisan to characterize the interaction between TRX and the remaining two candidate proteins by repeating the method steps taught with regard to the

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TRX/TBP-2; this is because it is merely the duplication of steps with regard to elements having a common property (i.e., the ability to bind to TRX). By repeating the same method steps of screening “proteomic interactions” between TRX and the remaining two TRX-interacting proteins, the instant method of determining “proteomic interactions between at least one protein and a plurality of proteins” is made obvious.

The ordinary skilled artisan would have been motivated to measure the interaction of TRX and the remaining two candidate proteins in the presence and absence of redox modifiers because TRX is “one of the major components of the thiol reducing system and plays multiple roles in cellular process such as proliferation, apoptosis and gene expression” (see for example the Abstract of Nishiyama), and TRX clearly has important interactions with other proteins (e.g., TBP-2) that are regulated by redox state. Thus, the skilled artisan would be motivated to examine all of TRX’s known interactions under altered redox conditions to more fully determine its role in important cellular processes such as apoptosis, etc., under altered redox conditions. Absent evidence to the contrary, the skilled artisan would have had a reasonable expectation of success when examining the interaction between TRX and the remaining interaction candidates under different redox conditions, especially given the fact that such method steps had already worked for a third TRX-interacting protein (TBP-2).

Allowable Subject Matter

No claims are allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636



JAMES KETTER
PRIMARY EXAMINER